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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,453	10/22/2001	Brian G. Fox	09820.188	2389

7590 01/21/2004

Intellectual Property Department
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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/001,453	Applicant(s) FOX ET AL.	
	Examiner Tekchand Saidha	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/18/02

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) ____ is/are withdrawn from consideration.

5)☐ Claim(s) ____ is/are allowed.

6)☒ Claim(s) 1-30 is/are rejected.

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on ____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. ____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicants' sequence listing filed July 18, 2002, is acknowledged.

2. Claims 1-30 are pending and under consideration in this examination.

Claims 1-18 are drawn to a non-radioactive labeled acyl carrier protein. Claims 19-28 are drawn to a kit comprising non-radioactive labeled acyl carrier protein (and instructions for its use). Claims 29-30 are drawn to methods of making non-radioactive labeled (holo or acylated) acyl carrier protein.

3. ***Priority***

For prior art purposes, with no earlier claims to priority, the filing date of 10/22/01 for this application will be considered the priority date.

4. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. ***Claim Rejections - 35 USC 112*** (first paragraph)

Enablement

(b) Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *Escherichia coli* labeled apo or holo or acylated acyl carrier protein comprising a 77 amino acid sequence [Abita et al. Eur. J. Biochem. 23 (1971) : 412-420, IDS], wherein the non-radioactive labeled product is NitroTyr-ACP, Amino Tyr-ACP, or DansylaminoTyr-ACP does not reasonably provide enablement for (1) labeled apo or holo or acylated acyl carrier protein from <u>any source</u> and (2) wherein the non-radioactive labeled

product is not other than NitroTyr-ACP, Amino Tyr-ACP, or DansylaminoTyr-ACP. The method and the kit claims are also enabled to the same scope as the product, and as indicated above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988))[*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are [the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary].

The claims are drawn to encompass labeled apo or holo or acylated acyl carrier protein from any source and wherein the non-radioactive label can be any compound, or any fluorophore including fluorescein, rhodamine, FITC (?) or TRITC (?) & Texas Red, which have neither been known or shown by the Applicants to have properties of an effective label (non-radioactive).

The disclosure or description is limited to E. coli acyl carrier protein and labeling of non-radioactive compound resulting in the formation of NitroTyr-ACP, Amino Tyr-ACP, or DansylaminoTyr-ACP. Despite knowledge in the art for overexpression and recombinant production of holo or apo acyl carrier protein from *E. coli* [Hill et al. Protein Expression and Purification 6 : 394-400 (195); IDS] as well as the availability of the protein from other sources

[Prescott et al. Adv. Enzy. And Rel. Areas of Mol. Biol. 36 : 269-311 (1972), IDS], it would be beyond the reasonable expectations of a skilled artisan to translate the specific chemical modifications of ACP obtained from a single species (*E. coli*) by specific processes of nitration, reduction, dansylation and/or acylation (as per Table 3), to ACP species obtained from any source. This is because of the diverse ACP source(s) having varying structure and function depending upon its origin. Thus, when the new ACP which is of different structure and function (physico/chemical) is subjected to specific chemical modication(s) of amino acid(s) based upon the experimentation of *E. coli* ACP, the chances of success are unpredictable. Since it is not routine in the art to engage in experimentation to make such modifications in order to obtain a labeled acyl carrier protein from any source and use any compound for modification where the expectation "of success is unpredictable", the skilled artisan would require additional guidance in order to make and use the product, the kit and the method in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

6. ***Written Description***

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-30 are directed to labeled apo or holo or acylated acyl carrier protein from any source and wherein the non-radioactive label can be any compound, or any fluorophore including fluorescein, rhodamine, FITC (?) or TRITC (?)& Texas Red; a kit and methods based thereof.

Claims 1-30 are rejected under this section of 35 U.S.C. 112 because the claim is directed to a genus of labeled acyl carrier proteins (ACPs) obtained by numerous chemical modifications, kits and method thereof that are encompassed by the claims and for which no description is apparent. This is would include the genus of ACP from any source as well as the numerous chemical modifications or reactions that are not yet described. No description has been provided of such ACPs and the numerous chemical reactions to obtain labeled ACP encompassed by the claim. No information, beyond the characterization of *Escherichia coli* labeled apo or holo or acylated acyl carrier protein, wherein the non-radioactive labeled product is NitroTyr-ACP, Amino Tyr-ACP, or DansylaminoTyr-ACP (and kit and methods of making) has been provided by applicants which would indicate that they had possession of the claimed genus of labeled ACPs, kits and methods of making. The specification does not contain any disclosure of the function of all the labeled carrier proteins obtained from a combination of representative ACPS of the diverse species of the plant & animal kingdoms and there chemical modifications, within the scope of the claimed genus. The genus of ACPs used in the product or method (or kit) claimed is a large variable genus including ACPs and chemical modifications (or reactions) not yet characterized. The specification discloses only selected *Escherichia coli* labeled apo or holo or acylated acyl carrier proteins, & labeled product such as NitroTyr-ACP, Amino Tyr-ACP, or DansylaminoTyr-ACP or species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

7. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 8, 17 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 17 and 27 recite abbreviations which are unclear. The first use of such uncommon abbreviations must be spelled out, which may be abbreviated in the subsequent claims.

8. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1 & 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Abita et al. [Abita et al. Eur. J. Biochem. 23 (1971) : 412-420, IDS]. Abita et al. teach nitration of ACP and palmityl-acyl-carrier protein (see abstract and page 413, column 1, procedure for nitration). The nitrated molecule(s), reacting with the tyrosine form a yellow chromophore, which is a non-radioactive and detectable label. The claims are written so broadly as to be anticipated by the reference.

9. Claim 1-3, 5, 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Hill, R. et al. [Protein Expression and Purification, (1995) Vol. 6, No. 4, pp. 394-400]. Hill, R. et al. teach a synthetic gene of 237 bases encoding the 77-residue acyl carrier protein (ACP) from Escherichia coli, along with two mutant genes, ACP-I54V and ACP-A59V, were subcloned into the pET11a-pLysS E. coli overexpression system under the control of the bacteriophage T7 promoter. This efficient expression system and a simplified purification protocol yielded more than 120 mg/l of pure protein. The construct produced a mixture of holo-ACP and apo-ACP and two HPLC procedures were developed to separate the two species. This overexpression system allows cost-effective growths of **13C- and 15N-labeled** (non-radioactive) protein for structural and other studies on ACP. In the course of the work on the mutants of ACP, an apparent homologous recombination event led, in one case, to reversion to a wild-type protein, suggesting that precautions to prevent such reversion should be taken.

10. Claims 1-30 are rejected under 35 U.S.C. 102(b) as being anticipated Haas et al. [**Protein Expression and Purification** Volume 20, Issue 2 , November 2000, Pages 274-284]. Haas et al. teach an *Escherichia coli* acyl carrier protein (ACP) containing a single tyrosine residue at position 71. The combined o-nitration of apo-ACP Y71 by tetranitromethane and reduction to 3-aminotyrosyl-apo-ACP were performed to introduce a specific site for attachment of a dansyl fluorescent label. Conditions for purification and characterization of dansylaminotyrosyl-apo-ACP are reported. Dansylaminotyrosyl-apo-ACP was enzymatically phosphopantetheinylated and acylated in vitro with an overall ~30% yield of purified stearoyl-dansylaminotyrosyl-ACP starting from unmodified apo-ACP. The steady-state kinetic parameters kcat = 22 min-1 and KM = 2.7 M were determined for reaction of stearoyl-

dansylaminotyrosyl-ACP with stearoyl-ACP 9-desaturase. These results show that dansylaminotyrosyl-ACP will function well for studying binding interactions with the 9-desaturase and suggest similar possibilities for other ACP-dependent enzymes. The efficient in vivo phosphopantetheinylation of E. coli apo-ACP by coexpression with holo-ACP synthase in E. coli BL21(DE3) using fructose as the carbon source is also reported. Detailed method steps are described for making non-radioactive labeled holo-ACP or acylated-ACP. The kit comprising the modified ACPs is inherent in the teachings of Haas et al. Therefore, the reference anticipates the claims.

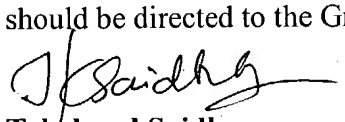
The cited reference (Applicants' own work) is applied under 35 U.S.C. 102(b), since the exact day in November, the article was published is not apparent from the publication. If the Applicants' contend that the cited reference should be applied under 35 U.S.C. 102(a), appropriate evidence must be provided.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



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